UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,512	05/05/2000	MICHAEL ANTHONY JOHNSON	2-00US	2004

23713 7590 08/27/2003

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER	
WINKLER, ULRIKE	
ART UNIT	PAPER NUMBER
1648	28

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/485,512	JOHNSON ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,25-32,39-42 and 44-62* is/are pending in the application.

4a) Of the above claim(s) *45-50 and 52-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,25-32,39-42,44 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *25* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed on April 1, 2003 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/485,512is acceptable and a RCE has been established.

The Amendment filed June 12, 2003 (Paper No. 27) in response to the Office Action of January October 1, 2002 and the personal Interview of June 11, 2003 (Paper NO. 26) is acknowledged and has been entered. Claims 1, 2, 4, 25-32, 39-44 and 51 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 25, is attached to the instant Office action.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 4, 25-32, 39-42,43 and 44 under 35 U.S.C. 103(a) as being unpatentable over either Callebrant et al. (Cornaviruses 1994,see IDS paper No. 6) or Torres et al. (Journal of Virology 1996, see IDS paper No. 6) and either Kleiboeker (Virus Research, 1994, see IDS paper No. 6) or Reddy et al. (Virus Research 1996, see IDS paper No. 6) **is withdrawn** in view of applicant's arguments and the 37 C.F.R. 1.132 declaration of Jeffrey Hammond (Paper No. 24).

The rejection of claims 1, 2, 4, 25-32, 39-42,44 and 51 under 35 U.S.C. 103(a) as being unpatentable over either Callebrant et al. (Cornaviruses 1994,see IDS paper No. 6) or Torres et al. (Journal of Virology 1996, see IDS paper No. 6) and either Kleiboeker (Virus Research, 1994, see IDS paper No. 6) or Reddy et al. (Virus Research 1996, see IDS paper No. 6) and further in view of Koneig et al. (Journal of Virology, 1995) **is withdrawn** in view of applicant's arguments and the 37 C.F.R. 1.132 declaration of Jeffrey Hammond (Paper No. 24).

New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 25-32, 39-42, 44 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a recombinant porcine adenoviral vector capable of expressing heterologous gene sequence. The specification has shown the insertion of heterologous sequences into the right hand region or E3 region of PAV 3. However, the claims are broadly drawn to include sites of insertion of heterologous DNA at any point in the adenovirus region including the E1 and E4 regions, which have not been sufficiently described in terms of their structure.

The 37 C.F.R. 1.132 Declaration of Jeffrey Hammond (Paper No. 24) explained that applicants have constructed a major late promoter-leader sequence expression cassette which is includes sequences from the tri-partite leader sequences, these leader sequences are found spread over a kilo base region of the genome which differs from the human adenoviral genome. Because of this difference between human and porcine adenovirus sequences, the structure of the human adenovirus does not provide sufficient structural information to determine the function of porcine adenovirus. The declaration indicates that it is necessary to have an understanding of the structure of the porcine adenovirus in order to determine the major late promoter and the requisite leader sequences. This sequences information was not available in the art at the time of filing. Applicants in their instant specification have provided the necessary structural information to produce a major late promoter (MLP) cassette which they used for the homologues recombination in order to produce porcine adenoviral vector with a heterologous sequence inserted. The declaration goes onto explain that homologues recombination for porcine adenoviruses, unexpectedly requires the use of a primary pig kidney cell line although the virus grows well in PK15 cells. Because the cells grow well in the PK15 cells, the need to process the constructs in a primary pig kidney cell is not obvious. To summarize the declaration clearly sets out that (1) knowledge of the structure of the tri-partite leader and major late promoter is required (2) and the requirement for processing through primary pig kidney cells.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making

the claimed product, or any combination thereof. In this case, the only factor in the specification is a partial structure in the form of the major late promoter and tripartite leader sequence. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus which reads on all porcine adenoviruses discovered and those yet to be discovered. Furthermore, at the time of filing there was no information in the art or in the specification regarding sequences of complete PAV genomes, this information is necessary to insert heterologous genes into regions other than the PAV E3 or right hand genome region disclosed. In order for homologous recombination to take place the key requirement is the alignment of homologous sequences in two DNA molecules, in the is case these sequences will be present in the wild type virus and they will also need to be present in the shuttle vector providing the heterologous sequence of interest which is to be inserted into the porcine adenovirus. To create the appropriate shuttle vector requires structural knowledge f the region into which the heterologous sequence is to be inserted.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus porcine adenovirus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method

of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

A definition by function alone "does not suffice, to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lily, 119 F.3 at 1568, 43 USPQ2d at 1406.

> It means little to "invent" a method if one does; not have possession of a substance that is essential to practicing that method. Without that substance, the claimed invention is more theoretical than real; it is, as defendants argue, akin to "inventing" a cure for cancer by utilizing a substance that attacks and destroys cancer cells while leaving healthy cells alone. Without possession of such a substance, such a cure is illusory, and there is no meaningful possessions of the method. (see 00-CV-6161, March 5th 2003 decision, United States District Court Western District of New York, Judge Larimer).

Based on the requirement for the structural knowledge regarding the insertion points in the porcine adenoviral vector, the instant invention does not provide a sufficient written description for insertion into regions other than the E3 or right hand genome region or for the use of another promoter cassette. Therefore, the instant specification does not provide sufficient written description for the breadth of the claimed invention.

Claims 1, 2, 4, 25-32, 39-42, 44 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a recombinant porcine adenoviral vector capable of expressing a heterologous gene sequence. The specification has shown the insertion

of heterologous sequences into the right hand genome or E3 region of PAV 3. However, the claims are broadly drawn to include sites of insertion of heterologous DNA at any point in the adenovirus including the E1 and E4 regions.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples , (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those n the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant specification provides the information regarding the PAV-3 tri-partite leader sequences which are different in size and location to the human adenoviruses. The 37 C.F.R. 1.132 declaration of Jeffrey Hammond (Paper No. 24) indicated that for successful production of porcine adenovirus expressing a heterologous gene (1) knowledge of the structure of the tri-partite leader and major late promoter is required (2) and there is the requirement for processing through primary pig kidney cells. The declaration indicates that it is necessary to have an understanding of the structure of the porcine adenovirus in order to determine sequences of the major late promoter and the requisite leader sequences. These sequences where not available in the art at the time of filing. Applicants in their instant specification have provided the necessary structures in order to produce a major late promoter cassette of PAV-3, which they used for the homologues recombination in order to produce porcine adenoviral vector that has a heterologous gene sequence inserted. Neither the specification or the prior art have provide the requisite knowledge regarding the structure of a complete PAV genome or the structure of other PAV

genomes, this information would be required if applicants intend to insert heterologous genes into regions other than the PAV region disclosed. In order for homologous recombination to take place the key requirement is the alignment of homologous sequences in two DNA molecules, in the is case these sequences will be present in the wild type virus and they will also need to be present in the shuttle vector providing the heterologous sequence of interest which is to be inserted into the porcine adenovirus. To create the appropriate shuttle vector requires structural knowledge of the region into which the heterologous sequence is to be inserted.

> It must be remembered, however, that"[p]atent protection is granted in return for an enabling disclosure sure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute an enabling disclosure." *Genentech. Inc.* v. *Novo Nordisk A/S,* 1O8 F83d 1361, 1365 (Fed. Cir.), cert denied, 522 U.S. 963 (1997) at 1366 (quoting *Brenner* v. *Manson,* 383 U.S. 519, 536 (1966) (stating, in context of the utility requirement that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"). Thus, while the need for some experimentation is by no means necessarily fatal, "reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Id.*

Thus, the lack of working examples for any other insertion site in the porcine adenovirus, lack of guidance regarding the structure of the porcine adenoviral genome in the specification and the prior art, and the great breadth of the claims greatly reduces the probability that one of skill in the art would successfully obtain the claimed invention without undue experimentation.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 8/25/03